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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/580,602 | 05/25/2006 | Robert Boizel | MERCK-2822 | 4960 |

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| EXAMINER | |
|---|---|
| BLAND, LAYLA D | |
| **ART UNIT** | **PAPER NUMBER** |
| 1623 | |

| MAIL DATE | DELIVERY MODE |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/580,602 | BOIZEL ET AL. | |
| | Examiner | Art Unit | |
| | Layla Bland | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-19,23-25 and 34-41* is/are pending in the application.

4a) Of the above claim(s) *7,12 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8-11, 13-19, 23-25, 35-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This office action is a response to Applicant's amendment submitted November 2, 2007, wherein claims 1 and 14-17 are amended, claims 20-22 are cancelled, and new claims 38-41 are added.

In view of the cancellation of claims 20-22, all rejections made with respect to those claims in the previous office action are withdrawn.

In view of Applicant's amendment submitted November 2, 2007, the objection to the specification for lacking a brief description of drawings is withdrawn.

In view of Applicant's amendment submitted November 2, 2007, the objections to claims 1, 14, and 16 for informalities is withdrawn.

In view of Applicant's amendment submitted November 2, 2007, the rejection of claims 1-6, 8-11, 13-25, and 35-37 under 35 USC 112, first paragraph, for not being enabled for prevention of disorders associated with hyperuricemia, is withdrawn.

The following rejection of record is maintained and modified to include new claims 38-41:

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 8-11, 13-19, 23-25, and 35-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brunet, et al (WO 00/39113, published July 6, 2000) in view of Chen, et al. (WO 00/47209, published August 17, 2000).

Brunet et al. teach compounds of the same core structure as the instant application. The compounds are activators of the PPARα and PPARγ isoforms and exhibit hypolipidaemic and hypoglycaemic effects [page 2, lines 15-25]. The hypolipidaemic and hypoglycemic effect of the compounds result from their ability to activate the PPARa and PPARγ isoforms [page 33, lines 15-17]. Given as an exemplary compound [page 34, lines 12-15] and preferred species [page 10, lines 9 and 10] is Example 16b, (2E, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid, which is the species which applicant has elected in the instant application. To demonstrate the antidiabetic and hypolipidaemic activity of the compounds, mice were treated via oral administration of 100mg/kg/day of the compound of example 16 [page 34, lines 21-26].

Brunet et al. do not teach the treatment of hyperuricemia or associated disorders, or the lowering of the serum uric acid level of a subject.

Chen et al. teach that activators of PPARγ are useful for the treatment of gout and related disorders [page 2, lines 31-33]. Chen, et al. also teach methods for the treatment of diseases associated with hyperuricemia (defined by Pittman, et al. as a serum uric acid concentration above 7 mg per dL) and methods for modulating serum uric acid levels in a subject [page 3, lines 1-5 and 23-24]. The preferred dosage for administration of a high affinity PPARγ ligand is in the range of 0.05 mg/kg to about 20

mg/kg, more preferably 0.05 mg/kg to about 2 mg/kg, most preferably 0.05 mg/kg to 0.2 mg/kg per day [page 10, lines 12-15]. Administration may be provided in single or multiple dosages [page 10, lines 19-21].

It would have been obvious to one of ordinary skill in the art to use the compounds of Brunet et al. for the treatment of hyperuricemia and associated disorders. The skilled artisan would have been motivated to do so with an expectation of success because Chen et al. teach that activators of PPARγ are useful for the treatment of gout and related disorders and the compounds of Brunet et al. are PPARα and PPARγ activators. The exemplary compound of Brunet et al. (elected species in the instant application) meets the limitations of claims 1-6, 8-11, 13-25, and 35-37. The dosages suggested by Chen et al. are more than 90% lower than the 100 mg/kg/day used by Brunet, et al. for the study of in vivo antidiabetic and hypolipidaemic activity in mice and meet the limitation of claim 24.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one

of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### *Response to Arguments*

Applicant's arguments filed November 2, 2007 have been fully considered but they are not persuasive.

Applicant argues that because the compounds of Brunet et al. activate both PPARα and PPARγ, that the claims are not obvious.

Chen et al. teach that compounds which activate PPARγ are useful for the treatment of gout and modulation of serum uric acid levels in a subject. Brunet et al. teach that the instantly claimed compounds are PPARγ activators. Thus, it would have been obvious to use these compounds for the treatment of gout and modulation of serum uric acid levels. The assertion that Brunet's compounds may also have other activity does not negate the teaching that they activate PPARγ and thus can be used for the treatment of gout and modulation of serum uric acid levels.

### *Conclusion*

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Bland whose telephone number is (571) 272-9572. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Layla Bland
Patent Examiner
Art Unit 1623
December 20, 2007

Shaojia Anna Jiang

12/21/07

Supervisory Patent Examiner
Art Unit 1623
December 20, 2007